



King's Research Portal

DOI:

[10.1186/s12968-018-0493-4](https://doi.org/10.1186/s12968-018-0493-4)

Document Version

Peer reviewed version

[Link to publication record in King's Research Portal](#)

Citation for published version (APA):

Villa, A. D. M., Corsinovi, L., Ntalas, I., Milidonis, X., Scannell, C., Di Giovine, G., Child, N., Ferreira, C., Nazir, M. S., Karady, J., Eshja, E., De Francesco, V., Bettencourt, N., Schuster, A., Ismail, T. F., Razavi, R., & Chiribiri, A. (2018). Importance of operator training and rest perfusion on the diagnostic accuracy of stress perfusion cardiovascular magnetic resonance. *Journal of cardiovascular magnetic resonance : official journal of the Society for Cardiovascular Magnetic Resonance*, 20(1). <https://doi.org/10.1186/s12968-018-0493-4>

Citing this paper

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

General rights

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

Take down policy

If you believe that this document breaches copyright please contact librarypure@kcl.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

**Importance of operator training and rest perfusion
on the diagnostic accuracy of stress perfusion cardiovascular magnetic
resonance**

Adriana D.M. Villa MRes MD PhD*, Laura Corsinovi MD PhD*, Ioannis Ntalas
MD PhD, Xenios Milidonis PhD, Cian M. Scannell MRes, Gabriella Di Giovine
MD, Nicholas Child BM MRCP, Catarina Ferreira MD, Muhummad Sohaib
Nazir MBBS BSc MRCP FHEA, Julia Karady MD, Esmeralda Eshja MD, Viola De
Francesco MD, Nuno Bettencourt MD PhD, Andreas Schuster MD PhD MBA,
Tevfik F. Ismail MRCP PhD FSCMR, Reza Razavi MD PhD, Amedeo Chiribiri
MD PhD FSCMR

* The first 2 authors equally contributed to this study.

Adriana D.M. Villa

Institutional address: School of Imaging Sciences & Biomedical Engineering,
King's College London, King's Health Partners, St Thomas' Hospital, London,
SE1 7EH, United Kingdom.

Email: Adriana.villa@kcl.ac.uk

Laura Corsinovi

Institutional address: School of Imaging Sciences & Biomedical Engineering,
King's College London, King's Health Partners, St Thomas' Hospital, London,
SE1 7EH and Cardiology Department of the Basingstoke and North
Hampshire Hospital, Basingstoke, United Kingdom

26 Email: laura.corsinovi@gmail.com

27

28 Ioannis Ntalas

29 Institutional address: School of Imaging Sciences & Biomedical Engineering,

30 King's College London, King's Health Partners, St Thomas' Hospital, London,

31 SE1 7EH and Cardiology Department, St. Thomas' Hospital, Guy's and St

32 Thomas' NHS Foundation Trust, London, United Kingdom

33 Email: Ioannis.ntalas@gstt.nhs.uk

34

35 Xenios Milidonis

36 Institutional address: School of Imaging Sciences & Biomedical Engineering,

37 King's College London, King's Health Partners, St Thomas' Hospital, London,

38 SE1 7EH

39 Email: xenios.milidonis@kcl.ac.uk

40

41 Cian Scannell

42 Institutional address: School of Imaging Sciences & Biomedical Engineering,

43 King's College London, King's Health Partners, St Thomas' Hospital, London,

44 SE1 7EH

45 Email: cian.scannell@kcl.ac.uk

46

47 Gabriella Di Giovine

48 Institutional address: School of Imaging Sciences & Biomedical Engineering,

49 King's College London, King's Health Partners, St Thomas' Hospital, London,

50 SE1 7EH, United Kingdom

51 Email: digiovine.gabriella@gmail.com

52

53 Nicholas Child

54 Institutional address: School of Imaging Sciences & Biomedical Engineering,

55 King's College London, King's Health Partners, St Thomas' Hospital, London,

56 SE1 7EH, United Kingdom

57 Email: nick.child@gstt.nhs.uk

58

59 Catarina Ferreira

60 Institutional address: Faculdade de Ciências da Saúde CICS, UBI, Covilhã,

61 Portugal

62 Email: catarina.m.ferreira.cf@gmail.com

63

64 Muhummad Sohaib Nazir

65 Institutional address: School of Imaging Sciences & Biomedical Engineering,

66 King's College London, King's Health Partners, St Thomas' Hospital, London,

67 SE1 7EH, United Kingdom

68 Email: sohaib.nazir@kcl.ac.uk

69

70 Julia Karady

71 Institutional address: School of Imaging Sciences & Biomedical Engineering,

72 King's College London, King's Health Partners, St Thomas' Hospital, London,

73 SE1 7EH, United Kingdom

74 Email: karadyjulia@gmail.com

75

76 Esmeralda Eshja
77 Institutional address: Radiology Department, ICS Maugeri IRCCS, Pavia, Italy
78 Email: Esmeralda.eshja@gmail.com
79
80 Viola De Francesco
81 Institutional address: School of Imaging Sciences & Biomedical Engineering,
82 King's College London, King's Health Partners, St Thomas' Hospital, London,
83 SE1 7EH, United Kingdom
84 Email: viola.defrancesco@gmail.com
85
86 Nuno Bettencourt
87 Institutional address: Cardiovascular R&D Unit, Faculty of Medicine,
88 University of Porto, Portugal
89 Email: bettencourt.n@gmail.com
90
91 Andreas Schuster
92 Institutional address: Department of Cardiology, Royal North Shore Hospital,
93 The Kolling Institute, Northern Clinical School, University of Sydney, Sydney,
94 Australia and University Medical Center Göttingen, Department of
95 Cardiology and Pneumology, Georg-August University, Göttingen Germany
96 and German Center for Cardiovascular Research (DZHK), partner site
97 Göttingen, Göttingen, Germany
98 Email: andreas.schuster@med.uni-goettingen.de
99
100 Tevfik F. Ismail

101 Institutional address: School of Imaging Sciences & Biomedical Engineering,
102 King's College London, King's Health Partners, St Thomas' Hospital, London,
103 SE1 7EH, United Kingdom

104 Email: Tevfik.ismail@kcl.ac.uk

105

106 Reza Razavi

107 Institutional address: School of Imaging Sciences & Biomedical Engineering,
108 King's College London, King's Health Partners, St Thomas' Hospital, London,
109 SE1 7EH, United Kingdom

110 Email: reza.razavi@kcl.ac.uk

111

112 Amedeo Chiribiri

113 Institutional address: School of Imaging Sciences & Biomedical Engineering,
114 King's College London, King's Health Partners, St Thomas' Hospital, London,
115 SE1 7EH, United Kingdom

116 Email: Amedeo.chiribiri@kcl.ac.uk

117

118 Word count: 4,431

119

120 **Address for correspondence:**

121 Dr Amedeo Chiribiri MD PhD FSCMR

122 School of Imaging Sciences & Biomedical Engineering, King's College London,

123 King's Health Partners

124 4th Floor Lambeth Wing

125 St Thomas' Hospital

126 London SE1 7EH
127 United Kingdom
128 Phone: +44(0)20718 87242
129 Fax: +44(0)20718 85442
130 Email: amedeo.chiribiri@kcl.ac.uk
131

132 **Abstract**

133 **Background:** Clinical evaluation of stress perfusion cardiovascular magnetic
134 resonance (CMR) is currently based on visual assessment and has shown
135 high diagnostic accuracy in previous clinical trials, when performed by
136 expert readers or core laboratories. However, these results may not be
137 generalizable to clinical practice, particularly when less experienced readers
138 are concerned. Other factors, such as the level of training, the extent of
139 ischaemia, and image quality could affect the diagnostic accuracy. Moreover,
140 the role of rest images has not been clarified.

141 The aim of this study was to assess the diagnostic accuracy of visual
142 assessment for operators with different levels of training and the additional
143 value of rest perfusion imaging, and to compare visual assessment and
144 automated quantitative analysis in the assessment of coronary artery
145 disease (CAD).

146 **Methods:** We evaluated 53 patients with known or suspected CAD referred
147 for stress-perfusion CMR. Nine operators (equally divided in 3 levels of
148 competency) blindly reviewed each case twice with a 2-week interval, in a
149 randomised order, with and without rest images. Semi-automated Fermi
150 deconvolution was used for quantitative analysis and estimation of
151 myocardial perfusion reserve as the ratio of stress to rest perfusion
152 estimates.

153 **Results:** Level-3 operators correctly identified significant CAD in 83.6% of
154 the cases. This percentage dropped to 65.7% for Level-2 operators and to
155 55.7% for Level-1 operators ($p < 0.001$). Quantitative analysis correctly
156 identified CAD in 86.3% of the cases and was non-inferior to expert readers

157 (p=0.56). When rest images were available, a significantly higher level of
158 confidence was reported (p=0.022), but no significant differences in
159 diagnostic accuracy were measured (p=0.34).

160 **Conclusions:** Our study demonstrates that the level of training is the main
161 determinant of the diagnostic accuracy in the identification of CAD. Level-3
162 operators performed at levels comparable with the results from clinical
163 trials. Rest images did not significantly improve diagnostic accuracy, but
164 contributed to higher confidence in the results. Automated quantitative
165 analysis performed similarly to level-3 operators. This is of increasing
166 relevance as recent technical advances in image reconstruction and analysis
167 techniques are likely to permit the clinical translation of robust and fully
168 automated quantitative analysis into routine clinical practice.

169

170 **Keywords**

171 Cardiovascular Magnetic Resonance, Stress Perfusion Imaging, Coronary
172 Artery Disease, Quantitative assessment, Myocardial Ischemia, Diagnostic
173 Accuracy, Training.

174

175 **Abbreviation list**

176 AHA: American Heart Association

177 CAD: coronary artery disease

178 CME: Continuous medical education

179 CMR: Cardiovascular magnetic resonance

180 EACVI: European Association of Cardiovascular Imaging

181 ESC: European Society of Cardiology

- 182 LAD: left anterior descending coronary artery
- 183 LCX: left circumflex coronary artery
- 184 LGE: late gadolinium enhancement
- 185 MBF: myocardial blood flow
- 186 MPR: myocardial perfusion reserve
- 187 RCA: right coronary artery
- 188 SCMR: Society for Cardiovascular Magnetic Resonance

189 **Background**

190 Stress perfusion cardiovascular magnetic resonance (CMR) is increasingly
191 used for the evaluation of patients with known or suspected coronary artery
192 disease (CAD) and has a class I indication for patients at intermediate risk of
193 CAD according to recent guidelines[1,2].

194 Stress perfusion CMR has been shown to be highly accurate for the detection
195 of CAD, with sensitivity ranging from 75% to 91% and specificity ranging
196 from 59% to 87%[3-5]. It should be noted that in most of these studies,
197 visual assessment has been carried out either by a core laboratory or by
198 expert readers, and therefore the findings may not be generalizable to
199 routine clinical practice. As stress perfusion CMR gains acceptance and
200 becomes more available, it will inevitably be performed in lower volume and
201 less experienced centers.

202 Stress perfusion CMR is typically evaluated by visual assessment. This can be
203 influenced by the extent of ischemia and the presence of areas of relatively
204 preserved perfusion, which can be used as reference[6]. Moreover, image
205 artefacts can complicate the interpretation of the images. Dark rim artefacts,
206 which are commonly observed during stress perfusion, can be misdiagnosed
207 as subendocardial perfusion abnormalities[7], in particular when relatively
208 long acquisition times are used and spatial resolution is low. Moreover,
209 areas of infarction are frequently associated with delayed perfusion[8,9].
210 The simultaneous evaluation of stress and rest perfusion CMR and late
211 gadolinium enhancement (LGE) images is recommended to identify areas of
212 myocardial infarction and improve the specificity of the
213 interpretation[10,11], and to exclude imaging artefacts[10].

214 Additionally, it has been suggested that rest perfusion images could play an
215 important role in improving the identification of imaging artefacts when
216 signal abnormalities are present on both stress and rest images[10]. The
217 acquisition of rest images enables quantification of perfusion reserve, but
218 prolongs scan times and requires additional contrast dosing.

219 Stress perfusion CMR is complex to read and requires significant training
220 and experience, however, the impact of training and experience has not been
221 formally studied and as yet, there are no specific recommendations in
222 current guidelines, apart from stating that stress perfusion CMR should be
223 part of the training program for Level-2 readers[12]. It is hoped that fully
224 quantitative automated methods may help bridge training gaps and support
225 clinical decision making.

226 We sought to determine the importance of the level of operator training of
227 the diagnostic accuracy of stress perfusion CMR; the role of rest perfusion
228 images in the identification of imaging artefacts and in the correct detection
229 of CAD; and to systematically compare the results of visual assessment with
230 semi-automated quantitative analysis to determine its additional value.

231

232 **Methods**

233 Consecutive patients (n=53) referred for stress perfusion CMR for suspected
234 CAD were retrospectively included in the study. All patients had invasive
235 coronary angiography on the basis of the clinical indication within 1 month
236 of the CMR examination. Exclusion criteria were contraindications to CMR,
237 gadolinium-based contrast agents or adenosine. Patients with previous
238 coronary artery bypass grafting, hypertrophic cardiomyopathy, aortic

239 stenosis, or other primary myopathic or valvular disease were excluded. All
240 subjects gave written informed consent in accordance with ethical approval.
241 This study complies with the Declaration of Helsinki.

242

243 **Image acquisition**

244 CMR images were acquired using a 3T scanner (Achieva, Philips Medical
245 Systems, Beth, The Netherlands) equipped with 32-channel phased-array
246 cardiac coil. The protocol included functional assessment, adenosine stress
247 and rest first pass perfusion imaging, and LGE. The images were acquired
248 using standard acquisition protocols and in end-expiratory breath-hold. For
249 stress imaging, 140 µg/kg/min of adenosine was administered. Imaging
250 commenced 3 min after infusion initiation. A dual bolus (equal volumes of
251 0.0075 mmol/kg followed by 0.075 mmol/kg after a 20-s pause) of contrast
252 agent (gadobutrol/Gadovist, Schering, Germany) was injected at 4 ml/s by a
253 power injector[13]. For perfusion, a saturation recovery prepared gradient
254 echo pulse sequence accelerated with k-t sensitivity encoding acceleration
255 with 11 training profiles was used. Typical imaging parameters were: 3
256 short-axis slices covering standard American Heart Association (AHA)
257 segments[14], 120 acquired dynamics/slice, flip angle 20°, TR 2.5 ms, TE
258 1.25 ms, saturation pre-pulse recovery time 100 ms, pixel size 1.9x1.9 mm,
259 slice thickness 10 mm.

260 Typical imaging parameters for LGE imaging were: long and short axis to
261 fully cover the left ventricle, inversion recovery turbo field echo, flip angle
262 25°, TR 6 ms, TE 3 ms, pixel size 0.7x0.7 mm, slice thickness 10 mm.

263

264 **Operator selection**

265 Nine operators were chosen amongst the physicians working in our unit and
266 in other European institutions, on the basis of their level of competency,
267 according to the European Society of Cardiology (ESC)/European
268 Association of Cardiovascular Imaging (EACVI) training guidelines[12]. A
269 total of 9 operators, 3 for each competency level, were chosen; all operators
270 had recently obtained the ESC/EACVI certification (within 2 months) for the
271 appropriate level. In brief, level-1 competency ESC certification requires 20
272 continuous medical education (CME) hours, involvement in 50 CMR cases
273 and 1-month fellowship; level-2 requires at least 50 CME hours, involvement
274 in 150 clinical cases of which 25 must be perfusion studies, a minimum of 3-
275 months fellowship and the European CMR exam; level-3 requires at least 50
276 CME hours, involvement in 300 clinical cases of which a minimum of 50
277 must be perfusion studies, at least 12-months training and the European
278 CMR exam. Level-1 competency reflects core CMR training, level-2 is
279 required to report CMR studies with support from a Level-3 operator and
280 Level-3 is required to perform, interpret and report CMR studies fully
281 independently[12].

282

283 **Image analysis – visual assessment**

284 Each operator was asked to report each of the 53 scans twice over a 4-week
285 period, with a minimum interval of 2 weeks between first and second read.
286 The scans were anonymized and presented to the operator as a full dataset,
287 including stress and rest perfusion and LGE, or as reduced datasets,
288 including stress perfusion and LGE only. The full and reduced datasets were

289 analysed blinded to clinical and angiographic data and in a randomized
290 order on different days. The study flowchart can be seen in Figure 1.

291 Visual assessment of adenosine stress perfusion CMR and LGE images,
292 displayed side-by-side, was performed as per clinical practice, in accordance
293 with standardized CMR protocols[15]. A perfusion defect was defined as a
294 regional reduction in myocardial signal during LV first-pass of contrast
295 agent, not related to artefacts and not corresponding to an area of scar on
296 LGE images.

297 Operators were asked to fill an on-line standardized form and to identify
298 segments with inducible ischaemia, to identify the presence and
299 transmural of LGE[16], to identify the most likely culprit coronary artery
300 based on the standard AHA segmentation[14], and to grade their confidence
301 in the diagnosis and the perceived image quality.

302 The confidence was graded as: 0- very unconfident, 1- unconfident, 2-
303 confident, 3- very confident. The perceived image quality was graded as: 0-
304 poor, 1- moderate, 2- good, 3- excellent.

305 Coronary angiography results have been used as reference standard. The
306 threshold for coronary artery lumen stenosis was 70% diameter stenosis for
307 epicardial vessels. All invasive angiographic images have been reviewed by
308 consensus of expert operators.

309

310 **Image analysis – quantitative assessment**

311 A different operator, blinded to results of visual perfusion assessment and
312 other clinical/angiographic data, performed the segmentation of the images
313 for semi-automated quantitative analysis using software and methods

314 previously developed and validated by our group. Respiratory motion was
315 corrected using affine image registration by maximization of the joint
316 correlation between consecutive dynamics within an automatically
317 determined region of interest[17]. A temporal maximum intensity projection
318 was calculated to serve as a feature image for automatic contour delineation
319 method. The operator then manually optimized the automatically generated
320 contours to avoid partial volume effects at the endocardial and epicardial
321 border[17]. The intervention of the operator was limited to image
322 segmentation. Quantitative perfusion analysis was then automatically
323 performed by Fermi-constrained deconvolution according to the methods
324 described by Wilke et al[18] and Jerosch-Herold et al[19], optimised for
325 high-resolution pixel-wise analysis [20,21]. Myocardial perfusion reserve
326 (MPR) was calculated as the ratio between stress and rest myocardial blood
327 flow (MBF) estimates. Ischaemia was defined as segments with MPR<1.5,
328 according to previously validated criteria[22,23].

329

330 **Statistical analysis**

331 Continuous variables are presented as mean±standard deviation for
332 normally distributed variables and as median with interquartile range for
333 non-parametric data. Normality was assessed with Q-Q plots and the
334 Kolmogorov-Smirnov test. Continuous variables were compared using an
335 unpaired Student *t* test or the Wilcoxon rank-sum test, as appropriate, and
336 categorical data were compared between groups using the Fisher exact test
337 and Pearson chi-square test. The McNemar test was used for paired
338 dichotomous data. Two-tailed values of $p < 0.05$ were considered to be

339 statistically significant. One-way ANOVA was used to determine differences
340 between multiple groups. Bonferroni correction was used to account for
341 multiple testing.

342

343 **Results**

344 **Characteristics of the population**

345 The mean age of the population (n=53) was 60.6 ± 12.7 years. Demographic
346 data are shown in Table 1. The prevalence of CAD in the group of patients
347 included in the analysis was 30.2%, with 16/53 patients positive for CAD on
348 invasive coronary angiography. Left anterior descending (LAD) lesions were
349 identified in 9 (17%) of the cases; left circumflex (LCX) lesions in 8 (15.1%)
350 of the cases; and right coronary artery (RCA) in 13 (24.5%) of the cases.
351 Within the group of patients with CAD, 8 patients had 1-vessel disease
352 (50%), 5 patients 2-vessel disease (31.3%) and 3 patients 3-vessel disease
353 (18.8%).

354

355 **Impact of operator training on correct CAD identification**

356 There was a significant correlation between an operator's training level and
357 the rate of correct identification of CAD on a per patient level on visual
358 assessment. The diagnosis of Level-3 operators agreed with invasive
359 coronary angiography in $83.6 \pm 2.3\%$ of the cases, while this percentage
360 dropped to $65.7 \pm 4.3\%$ for Level-2 operators and to $55.7 \pm 5.3\%$ for Level-1
361 operators ($p < 0.001$ between the 3 groups)(Figure 2). A significant difference
362 in the agreement with angiography between different levels of training was
363 also observed in a sub-analysis per coronary territory ($p < 0.001$)(Figure 3).

364 When different perfusion territories were compared, the agreement
365 between CMR and coronary angiography was higher for the LAD territory,
366 followed by the LCX and by the RCA territories. The same trend was
367 observed in all groups of operators, regardless of the level of training
368 ($p<0.001$).

369 The sensitivity and specificity for operators of different levels of training are
370 reported in Figure 4. Level-1 operators showed high sensitivity ($86.5\pm6.1\%$)
371 and low specificity ($41.9\pm10.9\%$). Level-2 operators had a sensitivity of
372 $57.3\pm4.7\%$ and a specificity of $69.4\pm9.9\%$. Level-3 operators showed a
373 sensitivity of $71.9\pm13\%$ and a specificity of $88.7\pm6.7\%$ respectively. There
374 was a statistically significant difference for both sensitivity and specificity
375 between different levels of training ($p<0.001$)(Figure 4).

376

377 **Impact of rest perfusion on correct identification of CAD**

378 When rest images were available, there was no statistically significant
379 difference at all levels of training (Figure 5) and in the overall analysis
380 ($69.6\pm14.3\%$ vs $67.1\pm13.1\%$; $p=0.34$). However, when rest images were
381 available, a significantly higher level of confidence was reported by the
382 operators ($p=0.022$) and subjective image quality was scored at a higher
383 level ($p=0.012$).

384

385 **CAD classification**

386 Figure 6 shows a comparison between the extent of CAD identified by the
387 operators on CMR images in comparison with invasive coronary
388 angiography. An overestimation of the severity of CAD was observed in

389 Level-1 operators, regardless of the number of vessels with CAD. Despite
390 being more accurate, Level-2 and Level-3 operators significantly
391 underestimated the number of positive perfusion territories in patients with
392 multi-vessel CAD.

393

394 **Impact of quantitative analysis on correct CAD identification**

395 Quantitative analysis was successfully performed in 51 patients. In 2 cases of
396 patients without CAD, the automated algorithms failed and no results could
397 be calculated. In both cases, this was due to the low quality of the diluted
398 pre-bolus used for the estimation of the arterial input function. **Level-3**
399 **visual assessment of the 2 cases where quantification failed yielded the**
400 **correct diagnosis in both cases when both stress and rest images were made**
401 **available to the readers, and in 66% of interpretations when only stress**
402 **perfusion was made available to the readers.** Quantitative stress perfusion
403 CMR analysis agreed with the results of invasive angiography in 86.3% of the
404 cases, performing significantly better than Level-1 and Level-2 operators
405 ($p<0.001$). Level-3 visual assessment and quantitative analysis were not
406 significantly different ($p=0.56$)(Figure 2). Quantitative analysis had a
407 sensitivity of 68.8% and specificity of 94.3%. When the 2 cases in which
408 quantitative analysis failed are considered as a missed diagnosis, the
409 concordance of quantitative analysis with invasive angiography was 83%,
410 with a sensitivity of 68.8% and a specificity of 89.2%.

411

412 **Discussion**

413 This study has several important findings. Operator training and experience
414 had a significant impact on diagnostic accuracy. Only Level-3 trained
415 operators had an accuracy comparable with the results reported by large
416 clinical trials[3-5]. Rest images did not significantly improve the diagnostic
417 accuracy of stress perfusion CMR but, when available, contributed to a
418 significantly higher confidence of the operators in their reports and to a
419 higher perceived image quality, regardless of the level of training. Finally,
420 semi-automated quantitative analysis performed better than Level-1 and
421 Level-2 operators, but similarly to a Level-3 operator. Quantitative analysis
422 however failed in 2/53 cases due to technical reasons related to the
423 administration of a diluted pre-bolus. However, the same cases could be
424 analysed visually.

425 Stress perfusion CMR plays an increasingly important role in the evaluation
426 of patients with known or suspected CAD. Recent European guidelines
427 recommend the use of stress perfusion CMR in patients with suspected CAD
428 and intermediate pre-test probability, with a class 1 indication and level of
429 evidence A, similarly to stress echocardiography and nuclear imaging[1,2].
430 US guidelines recommend stress perfusion CMR with 2A indication[24],
431 particularly in specific subgroups of patients[25]. These indications are
432 based on the assumption that stress perfusion CMR is highly accurate for the
433 identification of CAD and compares favorably with other functional
434 modalities. In large trials and meta-analyses, the sensitivity ranged from
435 75%[3] to 91%[4] and specificity ranged from 59%[3] to 87%[5]. In the CE-
436 MARC study[26], sensitivity was 86.5% and specificity was 83.4%, and the
437 MR-IMPACT 2 trial[27] reported a sensitivity of 75% and a specificity of

438 59%. These wide intervals most likely represent the variability in study
439 design, the different prevalence of disease in different populations, and
440 variability in the criteria used for visual assessment.

441 The diagnostic accuracy of stress perfusion CMR reported in the literature is
442 often the result of visual assessment carried out by expert readers, which are
443 usually Level-3 operators and often are internationally recognized experts.

444 Our study demonstrates that the diagnostic accuracy varied significantly
445 amongst groups of readers with different levels of training, and reached
446 values comparable with those of large studies only in the group of Level-3
447 operators. These results confirm the high diagnostic accuracy of stress
448 perfusion CMR in comparison with coronary angiography, however clearly
449 indicate the need for Level-3 supervision when stress perfusion scans are
450 reported.

451 From the analysis of the sensitivity and specificity for the detection of CAD in
452 different groups, it emerges that Level-1 operators had high sensitivity
453 (86.5%). This came however at the cost of a reduced specificity (41.9%) and
454 rate of overall correct CAD detection (55.7%). Factors such as image quality
455 and the prevalence of dark rim artefacts, which can mimic the presence of
456 subendocardial perfusion defects, could have played a role. In comparison,
457 Level-3 operators under-called the disease (sensitivity 71.9%) but had a
458 high specificity (88.7%). All diagnostic investigations involve a trade-off
459 between sensitivity and specificity. At a population level and from a health-
460 economic perspective, we feel that the results achieved by Level 3 operators
461 represent a reasonable balance between the need to identify significant
462 coronary disease and the high specificity required to avoid increasing down-

stream investigation costs through increased referral for invasive coronary angiography. The work of Patel et al[28] highlights the need for better selection of patients for invasive investigation given the costs and potential morbidity incurred by this.

Our results support the recommendations from the ESC [12], which state that Level-1 operators hold the basic knowledge in CMR sufficient to select appropriate CMR indications and interpret CMR reports, but are not cleared to report CMR scans. This is reflected in our result by the fact that Level-1 operators demonstrated a very low diagnostic accuracy, with poor specificity for the presence of CAD. According to the ESC guidelines, Level-2 operators may actively perform and report CMR, but are not completely independent and should work under the supervision of a Level-3 expert. This is also supported by our results, since Level-2 operators were significantly less accurate than Level-3 operators. Level-3 operators instead performed to levels similar to those reported by studies such as the CEMARC[26].

It should be noted that the Society for Cardiovascular Magnetic Resonance (SCMR) guidelines on training[29] differ slightly from the ESC guidelines used in this study to define the level of training of the operators. According to the SCMR guidelines, Level-2 operators can independently report CMR scans, whereas Level-3 certification has more to do with being able to lead a CMR unit and perform research in the field. Both guidelines agree that Level-1 training is not sufficient to practice CMR.

487 It has been suggested that rest perfusion images play an important role in
488 improving the identification of imaging artefacts when signal abnormalities
489 are present on both stress and rest images[10]. When assessing stress
490 perfusion CMR visually, guidelines advise displaying both rest and stress
491 images side-by-side to identify correctly inducible perfusion defect and
492 artefacts[10,11].

493 In our study, we did not find any significant difference in the diagnostic
494 accuracy when rest images were available. Our findings mirror those of
495 Biglands et al[30]. However, when testing the operator confidence and the
496 perceived image quality, a statistically significant difference was noted when
497 both stress and rest images were available. The increased confidence was
498 more evident for Level-1 and Level-2 operators.

499 Interestingly, Level-1 operators reported a higher confidence score than
500 more experienced operators, despite lower overall accuracy. This could
501 reflect a cognitive bias, also known as the Dunning-Kruger effect[31].

502 The diagnostic usefulness of rest perfusion imaging resides in the finding of
503 “fixed perfusion defect” on both stress and rest images, which may be
504 related to artefacts or to areas of myocardial infarction. However, this may
505 be overcome when stress perfusion CMR is assessed visually side-by-side
506 with LGE, as per guidelines[11] and as in our study. Nevertheless, rest
507 perfusion imaging remains a fundamental requirement for perfusion
508 quantification and MPR estimation.

509

510 Semi-automated quantitative assessment performed better than Level-1 and
511 Level-2 operators and similarly to Level-3 operators for the detection of

512 CAD. The latter is in keeping with the results of several other studies that
513 reported high sensitivity and specificity for quantitative analysis, with
514 sensitivity ranging from 80%[22] to 94.4%[32] and specificity ranging from
515 81%[33] to 100%[34]. Previous studies from Patel et al[6] and Mordini et
516 al[35] compared quantitative with visual and semi-quantitative analysis and
517 demonstrated that quantitative analysis is superior to visual assessment and
518 semi-quantitative assessment in the detection of ischemia, and that
519 quantitative analysis is the most accurate method to measure the total
520 ischemic burden.

521 In the present study, quantitative analysis was performed using a semi-
522 automated method which requires user input to confirm the automated
523 segmentation of the images but eliminates inter-observer variability for
524 what concerns the quantification procedure. This is of increasing relevance
525 as recent technical advances in image reconstruction and analysis
526 techniques are likely to permit the clinical translation of robust and fully
527 automated quantitative analysis into routine clinical practice [36-39]. In our
528 study however, the dual bolus approach used for arterial input function
529 measurements failed in 2 subjects, impeding quantitative analysis. The
530 advent of dual sequences capable of a more accurate assessment of the
531 concentration of gadolinium in the main bolus input function may make the
532 use of dual bolus redundant in the near future[37,40].

533

534 **Limitations**

535 This study included a selected population with suspected CAD and we
536 excluded patients with primary cardiomyopathy. Thus, our results on

537 diagnostic accuracy do not include other patterns of perfusion
538 abnormalities, which may require even more experience to discern (e.g.,
539 microvascular dysfunction).

540 Moreover, we used an anatomical reference standard (invasive coronary
541 angiography) to compare operators' performances in interpreting a
542 functional test, while a functional reference standard (e.g., fractional flow
543 reserve) may be more appropriate.

544 Our results demonstrate that similarly accurate detection of CAD can be
545 achieved by Level-3 operators and by automated perfusion quantification.

546 Although our study was not powered to demonstrate the superiority of
547 quantitative analysis, this has been the subject of a recent study which has
548 reported very similar findings[30]. The non-inferiority of automated
549 quantification to expert visual reads, in combination with the prognostic
550 value of quantitative analysis[23] will facilitate more widespread adoption
551 of stress perfusion CMR by less experienced readers.

552 Finally, all stress perfusion CMR were acquired in a single center, using a 3T
553 Philips scanner and a high-resolution k-t sequence. This may not reflect the
554 standard clinical acquisition in other centres.

555

556 **Conclusions**

557 This study demonstrates that visual assessment of stress perfusion CMR is
558 challenging for Level-1 and Level-2 operators but accurate in the hands of
559 Level-3 operators. Our results highlight the importance of the
560 recommendations of the ESC/EACVI training guidelines in CMR, which
561 recommend independent reporting for Level-3 operators only and

562 supervised reporting for Level-2 trained operators. The availability of rest
563 perfusion images was associated with significantly higher confidence and
564 higher perceived image quality, regardless of the level of training of the
565 operator. Quantitative analysis performed similarly to Level-3 trained
566 operators and could represent, in the future, a valid alternative to visual
567 assessment.

568

569 **Acknowledgements**

570 This work was supported by the National Institute for Health Research
571 (NIHR) Cardiovascular Health Technology Cooperative (HTC) and
572 Biomedical Research Centre (BRC) awarded to Guy's & St Thomas' NHS
573 Foundation Trust in partnership with King's College London. The views
574 expressed are those of the author(s) and not necessarily those of the NHS,
575 the NIHR or the Department of Health. This work was additionally supported
576 by the Wellcome/EPSRC Centre for Medical Engineering at King's College
577 London [WT 203148/Z/16/Z].

578 We are grateful to the radiographers at the School of Biomedical Engineering
579 and Imaging Sciences at King's College London for their support in the
580 acquisition of the images.

581 MSN was funded through a fellowship from the Medical Research Council
582 [MR/P01979X/1].

583

584 **Declarations**

585 **Ethics approval and consent to participate:** All subjects gave written
586 informed consent in accordance with ethical approval (ethics 15/NS/0030,
587 NHS Grampians Regional Ethics Committee).

588 **Consent for publication:** Not applicable.

589 **Availability of data and materials:** Please contact author for data requests.

590 **Competing interests:** The authors declare that they have no competing
591 interests.

592 **Funding:** This work was supported by the National Institute for Health
593 Research (NIHR) Cardiovascular Health Technology Cooperative (HTC) and
594 Biomedical Research Centre (BRC) awarded to Guy's & St Thomas' NHS
595 Foundation Trust in partnership with King's College London. This work was
596 additionally supported by the Wellcome/EPSRC Centre for Medical
597 Engineering at King's College London [WT 203148/Z/16/Z]. MSN was
598 funded through a fellowship from the Medical Research Council
599 [MR/P01979X/1]. All funding bodies equally contributed to the collection,
600 analysis, and interpretation of the data and to the investigators' salaries
601 during the study.

602 **Authors' contribution:** ADMV, LC, NB and AC conceived the study and
603 participated in the study design and coordination. IN, GDG, NC, CF, MSN, JK,
604 ES, VDF and AS analysed the data. ADMV, LC, XM, CS and TFI performed the
605 data analysis. AC segmented the data for quantitative analysis. ADMV and LC
606 drafted the manuscript. All authors critically revised the manuscript for
607 important intellectual content, read and approved the final manuscript.

608 **Authors' information:** Not applicable.

609 **Endnotes:** Not applicable.

610

611 **References**

- 612 1. Task Force Members, Montalescot G, Sechtem U, Andreotti F, Arden C,
613 Budaj A, et al. 2013 ESC guidelines on the management of stable coronary
614 artery disease: The Task Force on the management of stable coronary artery
615 disease of the European Society of Cardiology. *European Heart Journal*.
616 2013;34:2949–3003.
- 617 2. Authors Task Force members, Kolh P, Alfonso F, Collet J-P, Cremer J, Falk
618 V, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization.
619 *European Heart Journal*. The Oxford University Press; 2014;35:ehu278–619.
- 620 3. Schwitter J, Wacker CM, Wilke N, Al-Saadi N, Sauer E, Huettle K, et al.
621 Superior diagnostic performance of perfusion-cardiovascular magnetic
622 resonance versus SPECT to detect coronary artery disease: The secondary
623 endpoints of the multicenter multivendor MR-IMPACT II (Magnetic
624 Resonance Imaging for Myocardial Perfusion Assessment in Coronary Artery
625 Disease Trial). *J Cardiovasc Magn Reson. Journal of Cardiovascular Magnetic*
626 *Resonance*; 2012;14:1–1.
- 627 4. Nandalur KR, Dwamena BA, Choudhri AF, Nandalur MR, Carlos RC.
628 Diagnostic Performance of Stress Cardiac Magnetic Resonance Imaging in
629 the Detection of Coronary Artery Disease. *J Am Coll Cardiol*. 2007;50:1343–
630 53.
- 631 5. Li M, Zhou T, Yang L-F, Peng Z-H, Ding J, Sun G. Diagnostic accuracy of
632 myocardial magnetic resonance perfusion to diagnose ischemic stenosis
633 with fractional flow reserve as reference: systematic review and meta-
634 analysis. *JACC: Cardiovascular Imaging*. 2014;7:1098–105.
- 635 6. Patel AR, Antkowiak PF, Nandalur KR, West AM, Salerno M, Arora V, et al.
636 Assessment of advanced coronary artery disease: advantages of quantitative
637 cardiac magnetic resonance perfusion analysis. *J Am Coll Cardiol*.
638 2010;56:561–9.
- 639 7. Ferreira PF, Gatehouse PD, Mohiaddin RH, Firmin DN. Cardiovascular
640 magnetic resonance artefacts. *J Cardiovasc Magn Reson*. 2013;15:41.
- 641 8. Chiribiri A, Leuzzi S, Conte MR, Bongioanni S, Bratis K, Olivotti L, et al. Rest
642 perfusion abnormalities in hypertrophic cardiomyopathy: correlation with
643 myocardial fibrosis and risk factors for sudden cardiac death. *Clinical*
644 *Radiology*. 2015;70:495–501.
- 645 9. Villa ADM, Sammut E, Zarinabad N, Carr-White G, Lee J, Bettencourt N, et
646 al. Microvascular ischemia in hypertrophic cardiomyopathy: new insights
647 from high-resolution combined quantification of perfusion and late
648 gadolinium enhancement. *J Cardiovasc Magn Reson*. 2016;18:4.

- 649 10. Klem I, Heitner JF, Shah DJ, Sketch MH, Behar V, Weinsaft J, et al.
650 Improved detection of coronary artery disease by stress perfusion
651 cardiovascular magnetic resonance with the use of delayed enhancement
652 infarction imaging. *J Am Coll Cardiol*. 2006;47:1630–8.
- 653 11. Schulz-Menger J, Bluemke DA, Bremerich J, Flamm SD, Fogel MA,
654 Friedrich MG, et al. Standardized image interpretation and post processing
655 in cardiovascular magnetic resonance: Society for Cardiovascular Magnetic
656 Resonance (SCMR) Board of Trustees Task Force on Standardized Post
657 Processing. *J Cardiovasc Magn Reson*. BioMed Central Ltd; 2013;15:35.
- 658 12. Plein S, Schulz-Menger J, Almeida A, Mahrholdt H, Rademakers F, Pennell
659 D, et al. Training and accreditation in cardiovascular magnetic resonance in
660 Europe: a position statement of the working group on cardiovascular
661 magnetic resonance of the European Society of Cardiology. *European Heart*
662 *Journal*. Oxford University Press; 2011;32:793–8.
- 663 13. Ishida M, Schuster A, Morton G, Chiribiri A, Hussain ST, Paul M, et al.
664 Development of a universal dual-bolus injection scheme for the quantitative
665 assessment of myocardial perfusion cardiovascular magnetic resonance. *J*
666 *Cardiovasc Magnetic Resonance*. 2011;13:28.
- 667 14. Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, et
668 al. Standardized Myocardial Segmentation and Nomenclature for
669 Tomographic Imaging of the Heart A Statement for Healthcare Professionals
670 From the Cardiac Imaging Committee of the Council on Clinical Cardiology of
671 the American Heart Association. *Int J Cardiovasc Imaging* [Internet].
672 Lippincott Williams & Wilkins; 2002;18:539–42. Available from:
673 <http://circ.ahajournals.org/cgi/doi/10.1161/hc0402.102975>
- 674 15. Kramer CM, Barkhausen J, Flamm SD, Kim RJ, Nagel E. Standardized
675 cardiovascular magnetic resonance (CMR) protocols 2013 update. *J*
676 *Cardiovasc Magnetic Resonance*. 2013;15:91.
- 677 16. Kim RJ, Wu E, Rafael A, Chen E-L, Parker MA, Simonetti O, et al. The Use
678 of Contrast-Enhanced Magnetic Resonance Imaging to Identify Reversible
679 Myocardial Dysfunction. *N Engl J Med*. 2000;343:1445–53.
- 680 17. Hautvast G, Chiribiri A, Zarinabad N, Schuster A, Breeuwer M, Nagel E.
681 Myocardial blood flow quantification from MRI by deconvolution using an
682 exponential approximation basis. *IEEE Trans Biomed Eng*. 2012;59:2060–7.
- 683 18. Wilke N, Jerosch-Herold M, Wang Y, Huang Y, Christensen BV, Stillman
684 AE, et al. Myocardial perfusion reserve: assessment with multisection,
685 quantitative, first-pass MR imaging. *Radiology*. 1997;204:373–84.
- 686 19. Jerosch-Herold M, Wilke N, Stillman AE. Magnetic resonance
687 quantification of the myocardial perfusion reserve with a Fermi function
688 model for constrained deconvolution. *Med Phys*. 1998;25:73–84.

- 689 20. Zarinabad N, Chiribiri A, Hautvast GLTF, Ishida M, Schuster A, Cvetkovic
690 Z, et al. Voxel-wise quantification of myocardial perfusion by cardiac
691 magnetic resonance. Feasibility and methods comparison. *Magnetic*
692 *Resonance in Medicine*. 2012;68:1994–2004.
- 693 21. Sammut E, Zarinabad N, Wesolowski R, Morton G, Chen Z, Sohal M, et al.
694 Feasibility of high-resolution quantitative perfusion analysis in patients with
695 heart failure. *J Cardiovasc Magn Reson*. 2015;17:13.
- 696 22. Lockie T, Ishida M, Perera D, Chiribiri A, De Silva K, Kozerke S, et al. High-
697 resolution magnetic resonance myocardial perfusion imaging at 3.0-Tesla to
698 detect hemodynamically significant coronary stenoses as determined by
699 fractional flow reserve. *J Am Coll Cardiol*. 2011;57:70–5.
- 700 23. Sammut EC, Villa ADM, Di Giovine G, Dancy L, Bosio F, Gibbs T, et al.
701 Prognostic Value of Quantitative Stress Perfusion Cardiac Magnetic
702 Resonance. *JACC: Cardiovascular Imaging*. 2017.
- 703 24. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, et al.
704 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis
705 and management of patients with stable ischemic heart disease: a report of
706 the American College of Cardiology Foundation/American Heart Association
707 task force on practice guidelines, and the American College of Physicians,
708 American Association for Thoracic Surgery, Preventive Cardiovascular
709 Nurses Association, Society for Cardiovascular Angiography and
710 Interventions, and Society of Thoracic Surgeons. *Circulation*. 2012. pp. e354–
711 471.
- 712 25. American College of Cardiology Foundation Task Force on Expert
713 Consensus Documents, Hundley WG, Bluemke DA, Finn JP, Flamm SD, Fogel
714 MA, et al. ACCF/ACR/AHA/NASCI/SCMR 2010 expert consensus document
715 on cardiovascular magnetic resonance: a report of the American College of
716 Cardiology Foundation Task Force on Expert Consensus Documents.
717 *Circulation*. 2010. pp. 2462–508.
- 718 26. Greenwood JP, Maredia N, Younger JF, Brown JM, Nixon J, Everett CC, et
719 al. Cardiovascular magnetic resonance and single-photon emission
720 computed tomography for diagnosis of coronary heart disease (CE-MARC): a
721 prospective trial. *The Lancet*. 2012;379:453–60.
- 722 27. Schwitter J, Wacker CM, Wilke N, Al-Saadi N, Sauer E, Huettler K, et al. MR-
723 IMPACT II: Magnetic Resonance Imaging for Myocardial Perfusion
724 Assessment in Coronary artery disease Trial: perfusion-cardiac magnetic
725 resonance vs. single-photon emission computed tomography for the
726 detection of coronary artery disease: a comparative multicentre,
727 multivendor trial. *European Heart Journal*. 2013;34:775–81.
- 728 28. Patel MR, Peterson ED, Dai D, Brennan JM, Redberg RF, Anderson HV, et
729 al. Low diagnostic yield of elective coronary angiography. *N Engl J Med*.
730 *Massachusetts Medical Society*; 2010;362:886–95.

731 29. Kim RJ, De Roos A, Fleck E, Higgins CB, Pohost GM, Prince M, et al.
732 Guidelines for training in Cardiovascular Magnetic Resonance (CMR). J
733 Cardiovasc Magn Reson. 2007. pp. 3–4.

734 30. Biglands JD, Ibraheem M, Magee DR, Radjenovic A, Plein S, Greenwood JP.
735 Quantitative Myocardial Perfusion Imaging Versus Visual Analysis in
736 Diagnosing Myocardial Ischemia: A CE-MARC Substudy. JACC:
737 Cardiovascular Imaging. JACC: Cardiovascular Imaging; 2018;11:711–8.

738 31. Kruger J, Dunning D. Unskilled and unaware of it: how difficulties in
739 recognizing one's own incompetence lead to inflated self-assessments. J Pers
740 Soc Psychol. 1999;77:1121–34.

741 32. Biglands JD, Magee DR, Sourbron SP, Plein S, Greenwood JP, Radjenovic
742 A. Comparison of the Diagnostic Performance of Four Quantitative
743 Myocardial Perfusion Estimation Methods Used in Cardiac MR Imaging: CE-
744 MARC Substudy. Radiology. Radiological Society of North America;
745 2015;275:393–402.

746 33. Morton G, Chiribiri A, Ishida M, Hussain ST, Schuster A, Indermuehle A, et
747 al. Quantification of Absolute Myocardial Perfusion in Patients With
748 Coronary Artery Disease: Comparison Between Cardiovascular Magnetic
749 Resonance and Positron Emission Tomography. J Am Coll Cardiol. Journal of
750 the American College of Cardiology; 2012;60:1546–55.

751 34. Bernhardt P, Walcher T, Rottbauer W, Wöhrle J. Quantification of
752 myocardial perfusion reserve at 1.5 and 3.0 Tesla: a comparison to fractional
753 flow reserve. Int J Cardiovasc Imaging. 2012;28:2049–56.

754 35. Mordini FE, Haddad T, Hsu LY, Kellman P, Lowrey TB, Aletras AH, et al.
755 Diagnostic accuracy of stress perfusion CMR in comparison with quantitative
756 coronary angiography: fully quantitative, semiquantitative, and qualitative
757 assessment. JACC: Cardiovascular Imaging. 2014;7:14–22.

758 36. Zarinabad N, Hautvast GLTF, Sammut E, Arujuna A, Breeuwer M, Nagel E,
759 et al. Effects of Tracer Arrival Time on the Accuracy of High-Resolution
760 (Voxel-Wise) Myocardial Perfusion Maps from Contrast-Enhanced First-Pass
761 Perfusion Magnetic Resonance. Biomedical Engineering, IEEE Transactions
762 on. IEEE; 2014;61:2499–506.

763 37. Kellman P, Hansen MS, Nielles Vallespin S, Nickander J, Themudo R,
764 Ugander M, et al. Myocardial perfusion cardiovascular magnetic resonance:
765 optimized dual sequence and reconstruction for quantification. J Cardiovasc
766 Magn Reson. 2017;19:43.

767 38. Jacobs M, Benovoy M, Chang L-C, Arai AE, Hsu LY. Evaluation of an
768 automated method for arterial input function detection for first-pass
769 myocardial perfusion cardiovascular magnetic resonance. J Cardiovasc Magn
770 Reson. 2016;18:17.

- 771 39. Hsu LY, Jacobs M, Benovoy M, Ta AD, Conn HM, Winkler S, et al.
772 Diagnostic Performance of Fully Automated Pixel-Wise Quantitative
773 Myocardial Perfusion Imaging by Cardiovascular Magnetic Resonance. JACC:
774 Cardiovascular Imaging. JACC: Cardiovascular Imaging; 2018;11:697–707.
- 775 40. Gatehouse P, Lyne J, Smith G, Pennell D, Firmin D. T2* effects in the dual-
776 sequence method for high-dose first-pass myocardial perfusion. Journal of
777 Magnetic Resonance Imaging. 2006;24:1168–71.
- 778

779 **Figure titles and legends**

780 **Figure 1.** Study flowchart.

781 CMR: cardiovascular magnetic resonance, LGE: late gadolinium
782 enhancement.

783

784 **Figure 2.** Percentage of correct coronary artery disease (CAD) identification
785 (diagnostic accuracy) for different levels of CMR training and using
786 quantitative assessment.

787 CAD: coronary artery disease, CMR: cardiovascular magnetic resonance.

788

789 **Figure 3.** Percentage of correct CAD identification (diagnostic accuracy)
790 stratified by coronary territory.

791 CAD: coronary artery disease, LAD: left anterior descending coronary artery,

792 LCX: left circumflex coronary artery, RCA: right coronary artery.

793

794 **Figure 4.** Sensitivity and specificity for level of CMR training. * denotes
795 statistically significant difference ($p < 0.001$) between sensitivity values. **
796 denotes statistically significant difference ($p < 0.001$) between specificity
797 values.

798 Sens: sensitivity, spec: specificity.

799

800 **Figure 5.** Percentage of correct identification of CAD (diagnostic accuracy)
801 using stress perfusion only or stress and rest images.

802 CAD: coronary artery disease.

803

804 **Figure 6.** CAD classification for different levels of CMR training.
805 CAD: coronary artery disease, 1VD: one-vessel disease, 2VD, two-vessel
806 disease, 3VD: three-vessel disease.
807